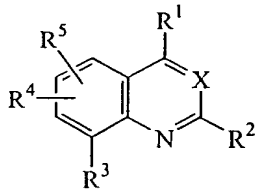
Claims

1. A compound of formula



(I),

including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein

X is N or CH;

R^1 is C_{1-6}alkyl, NR^6R^7, OR^7 or SR^7;

in case X is N then R^2 is hydrogen, C_{1-6}alkyl, C_{1-6}alkyloxy or C_{1-6}alkylthio;

in case X is CH then R^2 is C_{1-6}alkyl, C_{1-6}alkyloxy or C_{1-6}alkylthio;

R^3 is Ar^1 or Het^1;

R^4 and R^5 are each independently selected from hydrogen, halo, C_{1-6}alkyl, C_{1-6}alkyloxy, trifluoromethyl, cyano, nitro, amino, and mono- or di(C_{1-6}alkyl)amino;

R^6 is hydrogen, C_{1-8}alkyl, mono- or di(C_{3-6}cycloalkyl)methyl, C_{3-6}cycloalkyl, C_{3-6}alkenyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyloxyC_{1-6}alkyl or C_{1-6}alkyloxyC_{1-6}alkyl;

R^7 is C_{1-8}alkyl, mono- or di(C_{3-6}cycloalkyl)methyl, Ar^2CH_2, C_{1-6}alkyloxy-C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{3-6}alkenyl, thienylmethyl, furanylmethyl, C_{1-6}alkylthioC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, di(C_{1-6}alkyl)amino, C_{1-6}alkylcarbonylC_{1-6}alkyl;

or R^6 and R^7 taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, homopiperidinyl or morpholinyl group, optionally substituted with C_{1-6}alkyl or C_{1-6}alkyloxyC_{1-6}alkyl; and

Ar^1 is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C_{1-6}alkyl, trifluoromethyl, hydroxy, cyano, C_{1-6}alkyloxy, benzyloxy, C_{1-6}alkylthio, nitro, amino and mono- or di(C_{1-6}alkyl)amino;

Het^1 is pyridinyl; pyridinyl substituted with 1, 2 or 3 substituents each independently selected from halo, C_{1-6}alkyl, trifluoromethyl, hydroxy, cyano, C_{1-6}alkyloxy, benzyloxy, C_{1-6}alkylthio, nitro, amino, and mono- or di(C_{1-6}alkyl)amino; and

Ar^2 is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C_{1-6}alkyl, C_{1-6}alkyloxy, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, trifluoromethyl;

with the proviso that 2,4-dimethyl-8-(2-nitrophenyl)-quinoline is not included.

2. A compound according to claim 1 wherein R^1 is OR^7 or SR^7 and R^7 is C_{1-6}alkyl; or R^1 is NR^6R^7 and R^6 is hydrogen or C_{1-6}alkyl, and R^7 is C_{1-6}alkyl or C_{3-6}cycloalkylmethyl; R^2 is C_{1-6}alkyl; R^3 is a phenyl substituted with 1, 2 or 3 substituents each independently selected from C_{1-6}alkyl, C_{1-6}alkyloxy or halo, or R^3 is a pyridinyl substituted with 1, 2 or 3 substituents each independently selected from C_{1-6}alkyl or di(C_{1-6}alkyl)amino; and R^4 or R^5 are each independently selected from hydrogen or C_{1-6}alkyl.

3. A compound according to any of claims 1 to 2 wherein R^1 is NR^6R^7 wherein R^6 is C_{2-4}alkyl and R^7 is C_{2-4}alkyl or cyclopropylmethyl; R^2 is C_{1-2}alkyl; R^3 is phenyl substituted with 1, 2 or 3 substituents each independently selected from hydrogen, halo or C_{1-6}alkyl.

4. A compound according to any of claims 1 to 2 wherein R^1 is NR^6R^7 wherein R^6 is C_{3-4}alkyl and R^7 is C_{3-4}alkyl or cyclopropylmethyl; R^2 is methyl; R^3 is 3-pyridinyl substituted on the 4- and/or 6-position with methyl or dimethylamino.

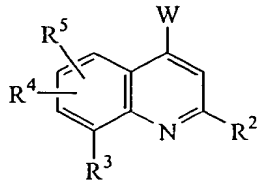
5. A compound according to claim 1 wherein the compound is 2-methyl-4-dipropylamino-8-(2',4'-dichlorophenyl)-quinoline; or 2-methyl-4-(*N*-propyl-*N*-cyclopropanemethyl)amino-8-(2',4'-dichlorophenyl)-quinoline; a stereoisomeric form or a pharmaceutically acceptable acid addition salt thereof.

6. A composition comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as claimed in any one of claims 1 to 5.

7. A process for preparing a composition as claimed in claim 6 wherein a therapeutically effective amount of a compound as claimed in any one of claims 1 to 5 is intimately mixed with a pharmaceutically acceptable carrier.

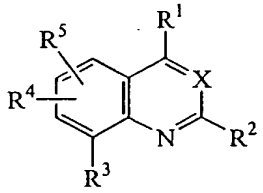
8. A compound according to any one of claims ~~1 to 5~~ for use as a medicine.

9. A compound of formula (II-a) wherein the radicals X, R^2, R^3, R^4 and R^5 are as defined in claim 1 and W is halo, mesyloxy or tosyloxy; a stereoisomeric form or an acid addition salt form thereof.



(II-a)

10. The use of compounds of formula

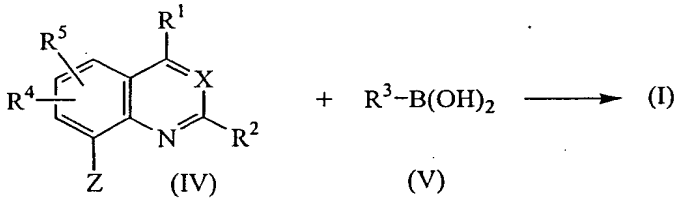


(I),

including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein X, R^1, R^2, R^3, R^4 and R^5 are as defined in claim 1, including the compound 2,4-dimethyl-8-(2-nitrophenyl)-quinoline, for the manufacture of a medicament for treating physiological conditions or disorders arising from the hypersecretion of corticotropin-releasing factor (CRF).

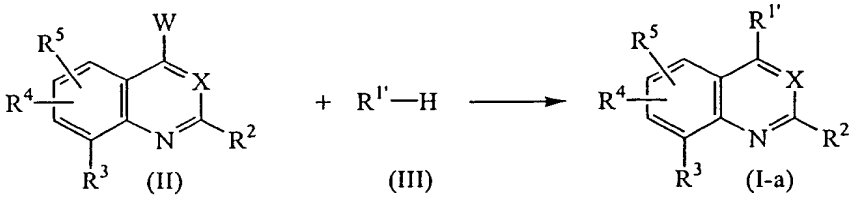
11. A process of preparing a compound of formula (I) as claimed in claim 1 wherein

a) intermediates of formula (IV) are reacted with intermediates of formula (V) under Suzuki coupling conditions;



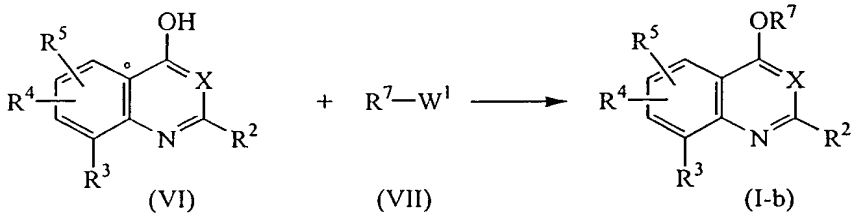
(IV) (V)

b) an intermediate of formula (II) is reacted with an intermediate of formula (III), wherein $R^{1'}$ has the meaning of R^1 other than C_{1-6}alkyl, thereby yielding compounds of formula (I-a);



(II) (III) (I-a)

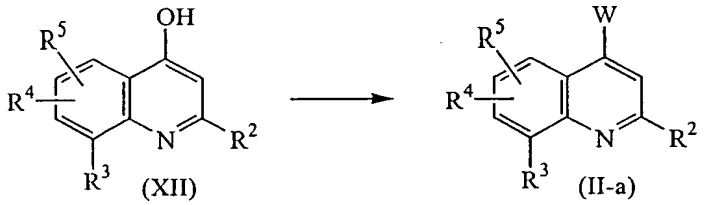
c) an intermediate of formula (VI) is *O*-alkylated with an intermediate of formula (VIIX) in a reaction-inert solvent and in the presence of a suitable base, yielding compounds of formula (I-b), defined as compounds of formula (I) wherein R^1 is OR^7,



wherein in the above reaction schemes the radicals R^1, R^2, R^3, R^6, R^7 and X are as defined in claim 1, Z is bromo or iodo and W and W^1 are appropriate leaving groups;

or, if desired, compounds of formula (I) are converted into each other following art-known transformation reactions; and further, if desired, compounds of formula (I) are converted into an acid addition salt by treatment with an acid, or conversely, the acid addition salt forms are converted into the free base by treatment with alkali; and, if desired, preparing stereochemically isomeric forms thereof.

12. A process of preparing a compound of formula (II-a) as claimed in claim 9 wherein a) an intermediate of formula (IX) is treated with methanesulfonyloxy chloride, benzenesulfonyloxy chloride or a halogenating reagent such as, e.g. $SOCl_2$ or $POCl_3$;



wherein in the above reaction scheme the radicals X, R^2, R^3, R^4 and R^5 are as defined in claim 1 and W is halo, mesyloxy or tosyloxy;

or, if desired, compounds of formula (II-a) are converted into each other following art-known transformation reactions; and further, if desired, compounds of formula (II-a) are converted into an acid addition salt by treatment with an acid, or conversely, the acid addition salt forms are converted into the free base by

treatment with alkali; and, if desired, preparing stereochemically isomeric forms thereof.

13. A method of antagonizing a CRF receptor in a warm-blooded animal, comprising administering to the animal an effective amount of a compound of any of claims 1 or 5.

14. A method of treating a disorder manifesting hypersecretion of CRF in a warm-blooded animal, comprising administering to the animal an effective amount of a compound of any of claims 1 or 5.

15. The method of claim 14 wherein the disorder is selected from depression, an anxiety-related disorder, a feeding disorder, stress-induced immune suppression, stroke, Cushing's disease, infantile spasms, epilepsy, seizure, an inflammatory condition.

16. The method of claim 15 wherein the feeding disorder is anorexia nervosa, bulimia or irritable bowel syndrome.